COMPARATIVE OUTCOMES AMONG THE PROBLEM AREAS OF INTERPERSONAL PSYCHOTHERAPY FOR DEPRESSION

by

Jessica C. Levenson

B.A., Brandeis University, 2004

Submitted to the Graduate Faculty of

Arts and Sciences in partial fulfillment

of the requirements for the degree of

Master of Science

University of Pittsburgh

2008

UNIVERSITY OF PITTSBURGH

ARTS AND SCIENCES

This thesis was presented

by

Jessica C. Levenson

It was defended on

September 4, 2008

and approved by

Ellen Frank, Ph.D., Distinguished University Professor, Psychiatry and Psychology

Jill Cyranowski, Ph.D., Assistant Professor, Psychiatry and Psychology

Daniel Shaw, Ph.D., Professor and Department Chair, Psychology

Andrew Koffmann, Ph.D., Clinical Associate Professor, Psychology

Thesis Advisor: Ellen Frank, Ph.D., Distinguished University Professor,

Psychiatry and Psychology

COMPARATIVE OUTCOMES AMONG THE PROBLEM AREAS OF INTERPERSONAL PSYCOHTHERAPY FOR DEPRESSION

Jessica C. Levenson, M.S.

University of Pittsburgh, 2008

While Interpersonal Psychotherapy (IPT) has proven to be an effective treatment for acute depression, the effectiveness of treatment in each of the four problem areas (grief, role transitions, role disputes, interpersonal deficits) has received little attention. The goal of this project was to provide some evidence for the specificity of IPT by comparing the success of treatment among patients whose treatment focused on each of the four problem areas. We hoped to understand how the patient characteristics and interpersonal problems most closely linked to the onset of an individual's current depression contributed to the success of IPT, with a particular emphasis on the role of personality pathology. In this sample of 181 individuals suffering from acute unipolar depression, chi-square analyses and the Wilcoxon Rank Sum Test indicated that the level of personality pathology reported by study participants was quite similar across all problem area groups. This was true when personality pathology was measured both continuously and categorically. Contrary to prediction, survival analyses indicated that patients in each of the four problem area groups demonstrated similar time to remission from their depression. The meaning and significance of these findings is described below.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

1.0 INTRODUCTION

1.1 SIGNIFICANCE

Depression is a pervasive, debilitating disorder that affects millions of individuals. The National Institute of Mental Health reported that about 9.5% of the population of the United States suffers from a depressive illness during any given year (2000). The World Health Organization (2007) reported that depression is one of the leading causes of disability worldwide, affecting nearly 121 million individuals. Despite the fact that depression can be reliably diagnosed and effectively treated, less than 25% of depression sufferers receive effective treatment (2007).

In an effort to provide relief for individuals who are afflicted with the disorder, several useful psychotherapies and pharmacotherapies have emerged in recent years. In addition to the more well known and widely disseminated cognitive and behavioral therapies (CBT; Beck, 1995; Beck, Rush, Shaw, & Emery, 1979; Leahy, 1996; Persons, Davidson, & Tompkins, 2000), interpersonal psychotherapy (IPT) has emerged as a

short-term, focused treatment whose effectiveness has been well supported by empirical research (Elkin et al., 1989; Frank et al., 1990; Frank, Kupfer, Wagner, McEachran, & Cornes, 1991; Klerman & Weissman, 1987; Reynolds et al., 1999).

However, there has also been an appeal to take a more critical look at the evidence for the specific efficacy of these therapies in recent years (e.g. Parker, Parker, Brotchie, & Stuart, 2006). In his review of psychotherapies, Wampold (2005) identified four phenomena that challenge the evidence of their utility: different psychotherapies actually produce similar results; there is a lack of evidence that supports specific effects of these psychotherapies; patients' improvement in these psychotherapies may be a result of common factors, not specific effects; and treatment outcome may be related to the level of the therapist's adherence to the psychotherapy. Thus, Parker and Fletcher (2007) argue that outcome research should move toward an understanding of the efficacy of psychotherapy treatment in specific contexts, not simply as a treatment of depression in general. This is the area of Wampold's findings on which we choose to focus.

Parker and Fletcher (2007) explain, "we acknowledge that […] IPT may nevertheless be specifically effective in some circumstances, but that evidence of such specificity still needs to be demonstrated – presumably in more context-specific clinical syndromes that respect the intrinsic logic of the specific therapy" (p. 357). They charge us to "identify those candidate disorders and aetiological circumstances that might best reflect the theoretical rationale for each therapy" (p. 357). Parker and colleagues (2006) also note that "the four interpersonal problem areas addressed in IPT […] have not been studied with respect to their outcome" (p. 7). They identify the need for such an investigation, given that the problem areas are a defining feature of IPT.

1.2 HISTORY

Interpersonal Psychotherapy (IPT) was developed by Gerald L. Klerman and collaborators in the late 1960's and was subsequently published as a manual-based treatment for depression (Klerman, Weissman, Rounsaville, & Chevron, 1984). IPT is a short-term, focused treatment for which strong empirical support has been developed since its inception (Elkin et al., 1989; Frank et al., 1990; Frank et al., 1991; Klerman & Weissman, 1987; Markowitz & Weissman, 2004; Reynolds et al., 1999; Weissman & Markowitz, 1994). Despite its logical outgrowth from the earlier work of the interpersonal school of psychotherapy, IPT in fact developed from a clinical trial rather than psychological theory. Within the research setting of the New Haven-Boston Collaborative Research Project, Klerman and colleagues completed a study using masters' level clinicians who conducted what the investigators thought would be a "placebo" contrast condition for pharmacotherapy. What they found was that the treatment was actually quite effective, thus leading to further investigation of this treatment and its elaboration and further specification as Interpersonal Psychotherapy (Weissman, 1994).

The theoretical basis for IPT follows from the work of Meyer and Sullivan, in which the social workers participating in the Boston-New Haven study were well schooled. Meyer emphasized the psychosocial features of an individual's environment

and the current experiences and social relations of the individual (Klerman et al., 1984). Harry Stack Sullivan, in his contribution to the interpersonal school of psychiatry, was influenced by Adolf Meyer's attention to the individual as the central unit of study (Sullivan, 1953). Sullivan defined psychiatry as the field of interpersonal relations, and noted that "there was an acute need for a discipline which was determined to study […] the interpersonal situations through which persons manifest mental health or mental disorder" (1953, p.18). Thus, we see the rationale behind Klerman and colleagues' (1984) conception of IPT as strongly rooted in the interpersonal school of psychiatry.

2.0 INTERPERSONAL APPROACH TO DEPRESSION

Even with Meyer and Sullivan's placement of psychiatric disorders in an interpersonal context, we still might ask, how are interpersonal problems related to depression? One viewpoint, and the viewpoint of IPT, holds that disturbances in social relationships can lead to clinical psychopathology. Klerman and colleagues (1984) focus on attachment, explaining that humans are at risk for developing impaired social relationships if attachment is not properly formed, while Bowlby (1982) states that we are also vulnerable to depression if existing attachments are damaged. He makes the point that disturbances in interpersonal relationships are capable of generating future mental health difficulties, thus linking interpersonal problems and psychopathology.

Life events and social support can also play a role in the development of depression. Life events that occur both in childhood and in adulthood are associated with the development of depression (Brown & Harris, 1978; Bifulco, Brown, & Harris, 1987; Harris, Brown, & Bifulco, 1986). Similarly, Leucken (2000) found that those who lost a parent during childhood have a greater likelihood of depressive symptoms as an adult;

however, these recent findings also suggest that the quality of social interaction and support that the individual experiences after the loss can impact the development of psychopathology in that individual later in life. As early as 1975, Weiss noted that deficient social bonds are associated with depression and neurosis in adults. Henderson and colleagues (1978) took this one step further, finding that not only is a lack of social bonds associated with the development of neurosis, but that this association was strongest with regard to one's most significant relationships.

Interpersonal disturbances are not the only factors related to depression; other factors such as genes, neurotransmitter levels, and other environmental stressors may also lead to the disease (National Institute of Mental Health, 2000). Nonetheless, the findings regarding social support, as well as the development of attachment and the disruption of existing attachments help to place depression in an interpersonal context. Parker's group summarizes this cogently: "underpinned by attachment, interpersonal and social theories, IPT assumes that an acute psychosocial stressor, in conjunction with insufficient social support, can lead to depressive symptoms" (Parker et al., 2006, p.2).

3.0 FORMAT OF INTERPERSONAL PSYCHOTHERAPY

Interpersonal psychotherapy aims to focus on the patient's[1] current depressive symptoms and interpersonal relationships, not those of the past (Klerman et al., 1984). At the outset of treatment a substantial amount of time is spent identifying the most significant people in the patient's life and describing the relationships among them, termed the interpersonal inventory (Klerman et al., 1984; Weissman, Markowitz, & Klerman, 2000). The underlying premise in IPT is that "disturbances in social roles can serve as antecedents for clinical psychopathology" (1984, p. 47); if the therapist and patient can remedy the interpersonal problem they may be able to reduce the resulting psychopathology (Markowitz, Bleiberg, Christos, & Levitan, 2006).

Treatment begins by reviewing the patient's symptoms, explaining how depression is treated using IPT, and assigning the "sick role" to the patient (Klerman et al., 1984). The therapist and patient then complete the interpersonal inventory. The initial sessions conclude with an assessment of the need for medication, an explanation of depression in a social context, and the therapist linking the patient's depression to his or her interpersonal situation (Klerman et al., 1984; Weissman et al., 2000).

[1] We will use the term 'patient' as opposed to 'client' here as this is consistent with the majority of the IPT literature, as well as the original IPT manual (Klerman, Weissman, Rounsaville & Chevron, 1984). See Stuart and Robertson (2003, p. x) for further explanation.

One of the ways the therapist explains the patient's depression in an interpersonal context is by assigning the patient's problems to one of four problem areas: grief, role transitions, role disputes, or interpersonal deficits. A patient's problems may fit into one or two problem areas, and the problem area focus may also change throughout the course of treatment (Weissman et al., 2000). The initial phase of treatment typically lasts 1-3 sessions, and concludes with the agreement of the patient and therapist as to which of the problem areas best addresses the patient's current distress. This process is a collaborative one, in which the therapist and patient temporally link the patient's current depressive episode to recent life events or other factors that may have contributed to the depression (Stuart & Robertson, 2003; Weissman et al., 2000).

At times, the patient and therapist may disagree about the most appropriate problem area; when this occurs, Weissman and colleagues (2000) suggest it may be necessary to accept the patient's goals temporarily. However, it is possible that the focus of treatment may later shift to the problem area that the therapist had originally felt was the best fit for the patient (2000); thus, therapy may continue despite initial disagreement.

The **grief** problem area focuses on "abnormal grief reactions that result from failure to progress through the various phases of the normal mourning process" (Klerman et al., 1984, pp.96-98). Work in this area aims to "facilitate the delayed mourning process" and "help the patient reestablish interests and relationships that can substitute for what has been lost" (Weissman et al., 2000, p. 64).

The **role disputes** problem area focuses on nonreciprocal role expectations that exist between the patient and one or more significant others in the patient's life (Klerman et al., 1984). For example, a patient who has chronic problems within her marriage may

conceptualize her distress as role disputes if this is the conflict that most closely led to her depression. The dispute might entail a disagreement over marital roles in the household. Klerman and colleagues note that role disputes can lead to depression because the feeling of losing control in the dispute can lead to a loss of self-esteem, in turn leading to depression. Thus, the therapist aims to help the patient "modify maladaptive communication patterns or reassess expectations" for the relevant relationship(s) (Klerman et al., 1984, p.105).

The **role transitions** problem area focuses on situations in which the patient has difficulty adapting to changes in key social roles, especially ones experienced as a loss; this difficulty can lead to feelings of helplessness and depressive symptoms in the patient (Klerman et al., 1984). Here, the therapist aims to help the patient experience the emotions associated with giving up the old role, attain new social skills and social supports (1984), and identify positive features of the new role (Weissman et al., 2000).

The **interpersonal deficits** problem area is assigned to those individuals who lack sufficient interpersonal relationships or who have difficulty maintaining the relationships that might exist (Klerman et al., 1984). This problem area is also assigned to patients who may have symptoms that were not adequately resolved in the past, and that interfere with current relationships (Weissman et al., 2000). The therapist reviews the patient's previous social relationships in order to identify common problems that arise in each; he or she then looks for similarities in the patient's relationship with the therapist, with the hope of modeling how to develop new rewarding relationships (1984). This problem area, more than the others, tends to explore some of the patient's past relationships, in addition to

existing ones (1984). In general, the problem area upon which the patient and therapist focus is typically the one that contributes most to the patient's depression (2000).

Once one of the problem areas is identified, the patient and therapist work collaboratively to resolve the pressing interpersonal problem, utilizing the appropriate strategies that correspond to each problem area (Klerman et al., 1984). The final phase focuses on preparing for termination, developing post-treatment coping strategies, and assessing the need for continuation treatment (1984). Typically, treatment for acute depression using IPT lasts 12 to 16 sessions in total (Markowitz & Weissman, 2004).

4.0 EFFICACY OF INTERPERSONAL PSYCHOTHERAPY

In general, IPT has proven to be equally effective, if not more effective, in treating acute depression as other treatment options (c.f.., Hollon et al., 2005). One of the earliest studies of acute depression examined IPT and amitriptyline, alone and in combination, as compared to a nonscheduled treatment control condition (Klerman & Weissman, 1987). This study found that each of the active treatments was more effective than the control treatment, while their combination was more effective than either treatment alone. However, at a one year follow-up, patients who had received IPT, alone or in combination, were functioning better than those who had received amitriptyline alone or nonscheduled psychotherapy (1987). This study essentially replicated results from an earlier study of amitriptyline and psychotherapy, described as weekly 50-minute sessions that were "short-term, interpersonal, and focused on the social context of the depression" (Weissman et al., 1979, p. 556). While the main findings of both studies were consistent, the earlier study also found that at a one-year follow-up, those patients who had received IPT during the acute phase, with or without pharmacotherapy, displayed significantly better social functioning than those who did not receive IPT (Weissman, Klerman, Prusoff, Sholomskas, & Padian, 1981).

Elkin and colleagues (1989) conducted a multi-site study of the effectiveness of four different treatments for depression in an outpatient setting: imipramine plus clinical management, IPT, cognitive-behavioral therapy (CBT), and placebo plus clinical management. In the overall sample, IPT fared as well as the other three treatments at reducing depressive symptoms. When analyzing patients with more severe levels of depression, both active medication and IPT were significantly more effective in reducing depressive symptomatology than placebo plus clinical management. The authors specifically note the clinical significance of how well IPT performed on the recovery criteria with the more functionally impaired patients (1989).

In addition to effectively treating acute depression, the interpersonal approach to treatment has made a valuable contribution as a maintenance treatment (IPT-M; e.g., Frank et al., 1991). While IPT's prophylactic effect as a maintenance treatment was not as strong as active imipramine, Frank and colleagues (1990) found that monthly sessions of IPT-M alone significantly lengthened the time between depressive episodes. Reynolds, Frank, and colleagues (1999) also showed that IPT-M and nortiptyline individually were superior to placebo in lengthening the time to recurrence, while the combination of IPT and the drug was superior to either treatment alone in older adults with depression. In a recent study (Frank et al., 2007), IPT-M was found to be an equally effective prophylactic treatment for depression in women, regardless of whether IPT was provided weekly, bi-weekly or monthly. However, maintenance IPT was less effective among women who had previously required the addition of pharmacotherapy to achieve initial remission (2007).

However, not all studies support the effectiveness of IPT above and beyond other treatments. For example, in a study of nortriptyline and IPT as treatments of bereavement-related depression in older adults, the authors found that there was no significant difference between IPT and placebo in effectiveness (Reynolds, Miller, et al., 1999) and Shear, Frank, Houck, & Reynolds (2005) found that classic IPT was less effective than a version specifically enhanced to address the needs of those with complicated grief. Nonetheless, there appears to be substantial evidence supporting the effectiveness of IPT in treating acute depression, as well as other psychological disorders.

Interestingly, thus far there appears to be only one study that examined the relationship between IPT problem area, probability of recovery, and patient characteristics (Wolfson et al., 1997). This study examined maintenance IPT in a population of elderly patients in which all patients received both IPT and nortriptyline as treatments. The authors found no significant differences in time to response among the problem areas; however, the interpersonal deficits group was excluded from analyses because of the small sample size (1997). Also, since all patients in this study received the drug we cannot attribute the changes in depressive symptoms to the IPT treatment alone.

Several studies involving IPT have shown that demographic and clinical variables are not related to long-term outcome of depression (Weissman, Prusoff, & Klerman, 1978) or time to remission (Bearden, Lavelle, Buysse, Karp, & Frank, 1996; Feske, Frank, Kupfer, Shea, & Weaver, 1998). In a study of maintenance IPT, Frank and colleagues (2007) reported that there were no significant differences among demographic or clinical characteristics between women requiring IPT and pharmacotherapy to achieve remission, and those requiring only IPT. However, the NIMH TDCRP suggested that

age, gender, and marital status were predictive of outcome within the four treatments examined in the study (IPT, CBT, imipramine plus clinical management, and placebo with clinical management; Sotsky et al., 1991). The authors noted, though, that there may have been a greater chance for findings in the study, given the size of the samples and the number of initial patient variables that were examined (1991).

5.0 INTERPERSONAL PSYCHOTHERAPY AND PERSONALITY

Some interesting work has also been conducted on the contribution of personality pathology to outcome in IPT, in part because of the frequent comorbidity of depression and personality disorders widely reported in the depression literature (e.g., Hirschfeld, 1999; Skodol et al., 1999). A number of researchers have explored the impact of personality disorders on the outcome of treatment for depression (Zuckerman, Prusoff, Weissman, & Padian, 1980; Shea et al., 1990; Bearden et al., 1996; Wolfson et al., 1997; Cyranowski et al., 2004). Not only has personality been associated with depression, it has also been identified as playing a role in the approach to IPT. As Stuart and Robertson (2003) explain, IPT views the patient's functioning "as a product of his or her temperament, personality, and attachment style […] in the context of social relationships and broad social support" (p. 4). These authors also note that the interpersonal deficits problem area, called interpersonal sensitivity by Stuart and Robertson, is often associated with personality disorders or avoidant personality traits. For these reasons we plan to explore the role of personality pathology as one of the patient characteristics affecting treatment success among patients in the four problem areas of IPT. The previous research conducted on the effect of personality on treatment for depression is described below.

In one analysis of the NIMH TDCRP (Elkin et al., 1989), Shea and colleagues (1990) found that although both those with personality disorders and those without showed a reduction in their depressive symptoms, those with personality disorders improved to a lesser degree and were more likely to have residual symptoms of depression. However, these differences were not statistically significant and were measured across all treatment conditions (1990).

In a study of IPT for depressed outpatients, Bearden and colleagues (1996) found that those with personality pathology were less likely to respond to IPT and those who did respond had a much longer time to remission. Cyranowski and colleagues (2004) examined the effect of personality pathology on treatment outcome using maintenance IPT for a group of depressed women. The results suggest that those with personality pathology experienced higher rates of recurrence and shorter time to recurrence than those who did not exhibit these symptoms (2004). While Luty, Joyce, Mulder, Sullivan, and McKenzie (1998) did not measure the influence of personality on treatment outcome, they noted that personality may have an effect on the patient's presenting problem area.

In summary, the general effectiveness of IPT for depression has been well supported, but the effectiveness of treatment in each of the four problem areas has received little attention. While many patients come to therapy for the treatment of depression, the life events and more chronic interpersonal personal problems associated with the onset of these depressive episodes differ, and are thus treated somewhat differently within the IPT framework. While we are confident in the efficacy of IPT overall, we want to ensure that a lack of improvement in one problem area is not being masked by excellent outcomes in another. In an effort to identify the specific contexts,

individual characteristics, and interpersonal problems that are best treated by IPT, we will compare the success of treatment among patients whose treatment focused on each of the four problem areas identified as possible foci of treatment in this therapeutic model. We aim to identify the specific problem areas in which IPT is more or less effective and the common personal characteristics of individuals in each area. To do so, we will compare patient factors that may differ from subject to subject in the population under study. We hope to provide some evidence for the specificity of IPT and to understand why one problem area may be more difficult to treat than another.

6.0 GOALS

One aim of this study is to understand how the interpersonal problem or problems most closely linked to the onset of an individual's current depression can contribute to the rate of success of IPT. We are interested to determine if characteristics unique to the individuals whose treatment is focused on each of the IPT problem areas contribute to the rate of IPT's success in reducing depressive symptomatology. One area we will explore in specific is the role of personality pathology; we expect that the group of individuals whose therapy focuses on interpersonal deficits will be more likely to have personality pathology that is comorbid to their depression than those whose therapy focuses on another problem area. If this additional pathology is present, perhaps it could help us to explain any differences in the rate of remission experienced in the interpersonal deficits group. Although we do not expect that demographic or clinical variables of the patients will be associated with time to remission, we will investigate these associations.

Similarly, situational influences may have an impact on individuals whose therapy focuses on the role disputes problem area. In this problem area, the depression is often the result of conflict between two individuals that leads to the role dispute, whereas in the other problem areas the focus is more squarely on the patient's difficulties. It may

be more difficult to resolve interpersonal problems when two individuals' needs must be taken into account, particularly if the other party to the dispute has no motivation to resolve it. In contrast, in situations in which it is more exclusively the patient's needs that are of significance, as in the case of grief or role transitions, therapeutic work may proceed more easily. Therefore, we expect that it would be more difficult for patients to achieve remission when their therapy focuses on role disputes than when the chosen problem area is role transition or unresolved grief.

We also expect that the interpersonal deficits problem area will be the most challenging problem area to treat, and that it will be associated with the longest time to remission. Patients whose therapy is focused on interpersonal deficits are described as having a history of social isolation, difficulty in forming and maintaining relationships with others, and are often more severely ill than patients in the other three problem areas (Stuart & Robertson, 2003; Weissman et al., 2000). Similarly, it is speculated that this problem area likely "carries the worst prognosis" (Markowitz & Swartz, 2007, p. 225) and may be better described as a long-standing attachment or personality style, rather than a response to a stressful life event (2003). Markowitz (2003) also notes that patients with interpersonal deficits may be more difficult to treat, explaining "One reason for this is that they are sicker patients, isolated and lacking in social supports, and more uncomfortable around other people, including their therapist. Another reason is that they lack the recent life events that IPT targets" (p. 849). As such, work in this problem area addresses more enduring pervasive problems in patients who may have more acute symptoms. Therefore, we expect that individuals whose therapy addresses interpersonal deficits will have a longer time to remission than the other three problem areas.

7.0 METHODS

7.1 PARTICIPANTS

This sample of 181 men and women was obtained from subjects participating in the study entitled, Depression: The Search for Treatment Relevant Phenotypes, Principal Investigator, Ellen Frank, Ph.D. Although 186 patients ultimately completed the study, at the time of analyses, data were available on only 181 of these patients. This two-site study was conducted at the University of Pittsburgh Medical Center's Depression and Manic Depression Prevention Program, part of the Western Psychiatric Institute and Clinic (WPIC), and at the Department of Psychiatry, Neurobiology, Pharmacology, and Biotechnology at the University of Pisa, Italy. Ninety-seven of the subjects were studied at the University of Pittsburgh, and 84 were studied at the University of Pisa.

The subjects ranged in age from 18 to 64 and met criteria for a current episode of non-psychotic unipolar major depression, as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR; American Psychiatric Association, 2000). This diagnosis was verified by the use of the Structured Clinical Interview for Axis I DSM-IV Disorders (SCID-I; First, Spitzer, Gibbon, &

Williams, 1997) and by a rating of 15 or greater on the 17-item Hamilton Rating Scale for Depression (HRSD-17; Hamilton, 1960). Patients who were already receiving effective treatment were not accepted into the study; additionally, the females were practicing an acceptable form of birth control and did not plan to become pregnant during the course of the study.

None of the subjects met the following exclusion criteria: a diagnosis of antisocial personality disorder, bipolar disorder, schizophrenia, schizoaffective disorder, or an organic affective disorder. They also did not meet criteria for drug and/or alcohol dependence in the three months preceding entry into the study, nor did they meet criteria for a primary diagnosis of anorexia nervosa or bulimia nervosa. The presence of an Axis II disorder was diagnosed using the Structured Clinical Interview for DSM-IV Personality Disorders (SCID-II; First, Gibbon, Spitzer, & Williams, 1997). Additionally, subjects who were previously intolerant of one of the study treatments, or who required inpatient treatment for psychosis or suicidal risk were excluded from the study.

In Pittsburgh, subjects were recruited through fliers distributed to WPIC clinics, medical professionals, and community organizations, and through public service announcements. At Pisa, because Italian law prohibits the announcement of clinical studies in public places or in the media, recruitment relied on the flow of patients attending the outpatient psychiatric clinic and on word of mouth. To increase participation, efforts were made to encourage referrals from primary care physicians.

7.2 PROCEDURES

Participants who entered into the study were randomly assigned to one of two conditions, psychotherapy or pharmacotherapy, which consisted of the SSRI escitalopram oxalate provided by a research psychiatrist. Those who were assigned to the psychotherapy condition, the 181 individuals in our sample, received IPT for approximately 45 to 50 minutes per week from their assigned therapist. At Pittsburgh, therapists were social workers, psychologists or nurse clinicians. At Pisa, therapists were recent graduates of the psychiatric residency training program. All therapists received training and supervision in IPT from an experienced research clinician, and they participated in regular group supervision at their respective sites throughout the course of the study.

After the first several sessions of IPT, the therapist and patient agreed upon a primary area of focus from among the four IPT problem areas. For some patients who were initially randomized to IPT, both a primary and a secondary problem area were agreed upon if it was felt that the patient's concerns would be better addressed by a broader conceptualization. In the overall sample roughly 70% of the participants were assigned a secondary problem area at least one time point. This is particularly important with regard to the interpersonal deficits area: if a patient's concerns fit this treatment focus, it was chosen as a secondary focus 50% of the time (n=11) as it is often easier to begin treatment with the grief, role disputes, or role transitions problem areas. However, this only occurred if the patient described problems that could also be addressed by exploring one of the other three problem areas, which was chosen as the primary focus. Given our hypothesis regarding those in the interpersonal deficits problem area, and the

fact that clinicians may be more likely to choose interpersonal deficits as a secondary problem area even if it is the main difficulty the patient is facing, we have defined the interpersonal deficits group as being comprised of any patient whose primary *or* secondary focus was identified as interpersonal deficits.

In this study, treatment "success" is measured by time to remission of depression in terms of days as it provides the most precise measure. Subjects were assessed weekly by an independent evaluator to measure their level of depressive symptoms. This evaluation was used at visit 7 to determine if *response* criteria had been met, defined as at least a 50% reduction of the baseline HRSD-17 score. If the criteria for improvement had not been met by visit 7, pharmacotherapy was added. If the response criteria *had* been met, subjects continued with IPT alone until visit 13, another triage point. At this point, patients were re-assessed to determine if stabilization criteria, or "remission," had been met; this was defined as a mean HRSD-17 score of 7 or below over a 3 week period. Again, if the criteria were not met at this point, escitalopram was added. This procedure was also carried out at visit 21, if stabilization or remission had not been met. If the subject met the initial response criteria by visit 7 but later worsened, and therefore did not meet stabilization criteria by either visit 13 or 21, escitalopram was added at one of these later points as well. An alternative pharmacotherapy strategy could be applied if the subject had not met stabilization criteria by visit 21.

Of those who received medication, the most common time points for the addition of escitalopram were visit 7 (58.0%) and visit 13 (10.1%). Although the majority of patients receiving medication began the treatment at one of the specified triage points, some individuals began pharmacotherapy at other time points throughout the study, as

medically indicated. Appropriately, individuals who had pharmacotherapy added to their treatment likely remained in the study longer both because their depression proved more difficult to treat, thus requiring medicine, and because of the additive design of the study.

Typically, a subject could remain in the acute phase of the protocol for a maximum of 32 weeks, even if remission had not been achieved by that point. Those who did not achieve remission by week 32 were evaluated to determine if continued treatment was clinically appropriate. If so, they could receive up to 64 weeks of treatment. This study will examine only those subjects who were initially assigned to the IPT condition, regardless of whether or not they required the addition of the pharmacotherapy treatment.

7.3 MEASURES

A diagnosis of depression was initially made using the Structured Clinical Interview for Axis I DSM-IV Disorders (SCID-I; First, Spitzer, et al., 1997) and a score of 15 or higher on the 17-item Hamilton Rating Scale for Depression (HRSD-17; Hamilton, 1960). The HRSD-17 was used to assess the severity of depressive symptoms at each clinic visit. Personality disorders were diagnosed using the Structured Clinical Interview for DSM Personality Disorders (SCID-II; First, Gibbon, et al., 1997), while level of personality pathology was measured by counting the sum of positive probes endorsed on the SCID-II. Both subthreshold and full threshold items that were endorsed on the SCID-II were counted in deriving the continuous score of personality pathology

for each patient as we wanted to take into account any personality pathology that may have been missed when identifying disorder diagnoses. In addition to depression, other Axis I disorders were also diagnosed using the SCID-I. When identifying these disorders, any diagnosis that met criteria for a current or lifetime full threshold disorder was included; subthreshold diagnoses were excluded as their effect on the treatment of depression may not have been as profound.

7.4 AIMS AND HYPOTHESES

The aim of the current study is to compare the groups of patients in each problem area on time to remission. As we expect that these groups will demonstrate significantly different times to remission, we hope to identify possible patient characteristics that may lead to these differences in success. We hypothesize:

1. Individuals whose therapy is focused on interpersonal deficits have more personality pathology, as measured by the sum of the individual probes endorsed on the SCID-II interview, than those whose therapy is focused on the other three problem areas.
2. Individuals whose therapy is focused on interpersonal deficits have more personality diagnoses, as assessed by the SCID-II interview, than those whose therapy is focused on the other three problem areas.

3. Individuals whose therapy is focused on interpersonal deficits have a longer time to remission (defined as 3 consecutive weeks during which the patient's HRSD-17 score averages ≤ 7), than those whose therapy is not focused on interpersonal deficits.

4. Individuals whose therapy is focused on role disputes have a longer time to remission, (defined as 3 consecutive weeks during which the patient's HRSD-17 score averages ≤ 7), than those whose therapy is focused on grief or role transitions.

7.5 DATA ANALYSES

Subjects initially assigned to the IPT condition were analyzed together using SPSS for windows; SAS for windows was utilized for one analysis of the Cox Proportional Hazard Model. Although conventional levels of statistical significance were set ($p \leq .05$), exploratory analyses were conducted on some results reaching a trend level ($p \leq .10$). Prior to testing the hypotheses, an analysis of variance (ANOVA) was conducted to test for differences among the four treatment focus groups on the demographic and clinical variables. Post-hoc tests were conducted to identify differences between the means of pairs of problem area groups using the Hochberg test. The Games-Howell test was substituted for comparisons in which the variances among the four groups were unequal, likely a result of the unequal sizes of each group. There was also some suggestion that the normality assumption was not met for a few of the continuous variables. Both parametric

and non-parametric tests were conducted with results indicating consistent findings. Thus, the ANOVA results are reported here.

The Cox Proportional Hazards Model was used to determine if any demographic or clinical variables or problem area assignment had an effect on time to remission; these variables were entered into the model together in two hierarchical steps. This model was also utilized to determine if the patient's level of personality pathology, measured continuously, and the addition of medication had an effect on time to remission when entered into the model alone. Here, the addition of medication was examined as a time-varying covariate as not all patients who received medication received it at the same time.

With regard to analyses conducted to test the four hypotheses, the chi-square test was utilized to compare the interpersonal deficits group and the combination of the other three problem area groups on the proportion of patients reporting at least one personality disorder. In order to compare these two groups of patients on the continuous level of personality pathology that they reported, the Wilcoxon Rank Sum Test was used. Kaplan-Meier survival curves were created to characterize the time to remission of the four problem area groups. The Log Rank Test was used to compare the interpersonal deficits group to the other three groups combined on time to remission, and to compare the role disputes to the grief and role transitions group on this measure.

Exploratory analyses were then conducted to examine possible differences between patients at each site regarding to time to remission and the demographic and clinical variables. Additionally, analyses were conducted to determine if the addition of medication was associated with any patient characteristics, or if the frequency or timing of the addition of this second treatment differed among the four problem area groups.

8.0 RESULTS

A summary of demographic information by problem area is listed in Table 1. The sample is made up primarily of Caucasian, well-educated females. An analysis of variance revealed that the four problem area groups differed on age (F=3.448, p=0.018), age at first depressive episode (F=3.673, p=0.013), the presence of at least one additional full threshold lifetime or current Axis I disorder (F=3.632, p=0.014), and the proportion of patients in each problem area group at each site (F=6.595, p=0.0001). Differences in the proportion of each group who were married did not reach conventional levels of statistical significance (F=2.292, p=0.08).

Based on these findings, post-hoc comparisons using the Hochberg and Games-Howell tests were conducted to identify differences between the means of pairs of problem area groups. These tests revealed that the role disputes group was older and more likely to be married than the role transitions group, while the role transitions group was more likely to have an additional Axis I disorder than the role disputes group. The results also showed that the role transitions group had an earlier age of first depressive episode than patients in the grief groups. These post-hoc comparisons reach a trend level of significance. Lastly, of patients whose treatment focused on role transitions,

Table 1. *Demographics and Clinical Characteristics of the Sample*

	Grief N=16	**Inter. Deficits N=22**	**Role Disputes N=72**	**Role Transitions N=71**	**All Groups N=181**	**F**
Mean Age (S.D.)	42.92 (3.21)	42.43 (2.69)	40.59 (1.45)	35.39 (1.49)	**38.98 (0.95)**	**3.448****
Sex (Female)	87.5%	63.6%	73.6%	64.8%	**70.2%**	**1.379**
Ethnicity (Caucasian)	75.0%	90.9%	94.4%	88.7%	**90.1%**	**1.938**
Mean Education Level in Years (S.D.)	13.67 (0.60)	13.41 (0.65)	13.82 (0.41)	14.74 (0.33)	**14.13 (0.24)**	**1.588**
Employed/Student	93.8%	81.8%	78.6%	74.6%	**78.8%**	**0.922**
Married or Living with a Partner	25.0%	36.4%	48.6%	29.6%	**37.6%**	**2.292***
Mean Age at First Episode (S.D.)	32.44 (4.10)	23.00 (2.76)	28.66 (1.46)	23.73 (1.36)	**26.35 (0.95)**	**3.673****
Mean Number of Previous Episodes (S.D.)	4.36 (2.60)	3.00 (0.78)	2.241 (0.19)	3.34 (0.49)	**2.98 (0.22)**	**1.291**
Medication Added	31.3%	36.4%	34.7%	45.1%	**38.7%**	**0.535**
Baseline HRSD-17 Score	19.94 (0.99)	19.41 (0.79)	19.86 (0.41)	19.51 (0.46)	**19.67 (3.67)**	**0.175**
Other Axis I Disorders	37.5%	54.5%	47.2%	70.4%	**56.4%**	**3.632****
One or more Axis II Disorders	33.3%	45.5%	31.9%	22.5%	**30.0%**	**1.537**
Site (Pittsburgh)	43.8%	40.9%	40.3%	73.2%	**53.6%**	**6.595****
Remitted	87.5%	72.7%	88.9%	78.9%	**82.9%**	**1.495**

*$p<0.10$

**$p<0.05$

significantly more of them participated in the study at Pittsburgh than patients whose treatment focused on role disputes.

With regard to the effect of demographic and clinical variables on time to remission, Table 2 outlines the results of a Cox Proportional Hazards model including these variables. At the first stage of the model age, sex, education level, marital status (married or living with a partner vs. not), ethnicity (Caucasian vs. not), and employment status (employed or a student vs. not) were entered into the model; patients reporting a higher level of education experienced a longer time to remission (Exp(*ß)*=0.931, *p*=0.015). Next, age at first depressive episode, number of previous depressive episodes, baseline HRSD-17 score, the presence of at least one additional full threshold current or lifetime Axis I disorder, the presence of at least one Axis II disorder, site, and problem area assignment were added to the model. At this stage, the effect of education diminished. However, patients in Pittsburgh (Exp(*ß)* =2.752, *p*=0.0001) and patients with a higher baseline HRSD-17 score (Exp(*ß)* =0.923, *p*=0.003) experienced a longer time to remission. Patients with at least one personality disorder also experienced a longer time to remission at a trend level (Exp(*ß)*=0.692, *p*=0.092).

It is important to keep in mind that, as Table 3 shows, site appears to be significantly correlated with a number of variables such as education, ethnicity, sex, education level, baseline HRSD-17 score, and the presence of an additional Axis I disorder. Thus, it is possible that at the second stage of the model site may be masking a potentially significant relationship between these variables and time to remission. Specifically, the significant relationship between education and time to remission diminished when site was added to the model.

Table 2. *Relationship between Demographic and Clinical Variables and Time to Remission using the Cox Proportional Hazards Model*

Model	***Variable***	**Exp(*ß*)**	***Significance***
(1)	Age	0.994	0.428
	Education	0.931	0.015*
	Sex	0.953	0.803
	Married	1.258	0.247
	Employed	1.010	0.967
	Ethnicity	0.769	0.416
(2)	Age	0.996	0.734
	Education	0.996	0.903
	Sex	1.033	0.874
	Married	1.341	0.146
	Employed	0.762	0.299
	Ethnicity	1.310	0.437
	Site	2.752	0.0001*
	Age at first episode	1.003	0.838
	Number of previous episodes	1.003	0.614
	Other Axis I Disorders	0.816	0.355
	One or more Axis II Disorders	0.696	0.092
	Problem Area	1.060	0.630
	HRSD-17	0.923	0.003*

* Variable is a significant predictor of time to remission

Table 3. *Correlations among Clinical and Demographic Variables*

	Site	Age	Educ.	Sex	Ethnicity	Married	Employed	Age at First Episode	# of Previous Episodes	Other Axis I Disorders	Axis II Disorders	HRSD-17
Site	-											
Age	-0.006	-										
Educ.	-0.499*	-0.011	-									
Sex	-0.219*	-0.065	0.154*	-								
Ethnicity	-0.205*	-0.034	0.014	0.140	-							
Married	0.079	0.405*	-0.072	-0.082	-0.143	-						
Employed	0.093	-0.268*	0.154*	0.073	-0.089	-0.100	-					
Age at First Episode	0.188*	0.471*	-0.151*	-0.032	-0.033	0.299*	-0.041	-				
# of Previous Episodes	-0.011	0.072	0.047	0.023	0.055	-0.026	-0.042	-0.363*	-			
Other Axis I Disorders	-0.298*	-0.040	0.164*	0.063	0.173*	0.016	-0.010	-0.244*	0.039	-		
Axis II Disorders	-0.022	-0.071	0.046	0.074	0.121	-0.103	0.016	-0.125	0.070	-0.064	-	
HRSD-17	0.065	0.144	-0.187*	-0.041	0.211*	0.010	-0.169*	0.064	0.023	0.010	-0.006	-

*$p<0.05$

Examining the potential differences among the groups on personality pathology, both categorical and continuous measures were used, as some patients may have had personality pathology that did not meet criteria for a specific diagnosis but that is nonetheless clinically significant. The first hypothesis states that individuals whose therapy is focused on interpersonal deficits have more personality pathology, as measured by the sum of the individual probes endorsed on the SCID-II interview, than those whose therapy is focused on the other three problem areas. The Wilcoxon Rank Sum Test showed that the interpersonal deficits group did not differ significantly from the other three problem area groups on mean level of personality pathology (W=14363.5, p=0.908). As the normality assumption was not met for the distribution of the personality pathology variable, shown by the Kolmogorov-Smirnov test (K-S=0.121, p=0.0001), the Wilcoxon Rank Sum test was utilized for this analysis. The second hypothesis states that individuals whose therapy is focused on interpersonal deficits have more personality diagnoses than those whose therapy is focused on the other three problem areas. Here, a chi-square test between these two groups of patients on the presence of one or more personality disorders revealed a non-significant trend (X^2=2.851, p=0.091) for higher likelihood of a personality diagnosis in the deficits group, as is shown in Table 1.

Of the 181 individuals included in the analysis of time to remission, 31 (17.1%) were considered censored observations. Of these, 24 (77.4%) were considered informative observations as the reason they did not remit seemed to be related to their depression. Examples include non-adherence to treatment, non-response to treatment, relapse, or being lost to follow-up. The remaining 7 (22.6%) individuals were considered non-informative observations; typical reasons for termination among this group included

relocating to a different city or a change in diagnosis. Thus, 150 patients achieved remission by the end of their time in the study.

In order to test the differential effectiveness of IPT based on our hypotheses Kaplan-Meier curves were created for each of the four groups. As Figure 1 demonstrates, the survival times among the four problem area groups are quite similar. The median time to remission among all participants was 81 days (roughly 11.6 weeks) with a standard error of 4.287 days. To test our third hypothesis, that individuals whose therapy is focused on interpersonal deficits have a longer time to remission than all other patients, Kaplan-Meier curves were created to show the survival times of the interpersonal deficits group and the other three groups combined. These curves are shown in Figure 2. The Log Rank Test was used to compare these two groups of participants on time to remission. Contrary to prediction, the interpersonal deficits group did not show a longer time to remission than the other three groups combined (X^2=0.438, p=0.508).

To test the fourth hypothesis, that individuals whose therapy is focused on role disputes have a longer time to remission than those whose therapy is focused on grief or role transitions combined, another set of Kaplan-Meier curves was created to show the times to remission of these two groups, as shown in Figure 3. The interpersonal deficits group was left out of this analysis; as it was originally hypothesized that this group would be more difficult to treat than the others, we compared only the role transitions and grief groups to the role disputes group as planned. These three groups share the similarity of typically experiencing a life event as a precipitant to their depression, while those in the deficits group typically do not. The Log Rank Test showed no difference in time to

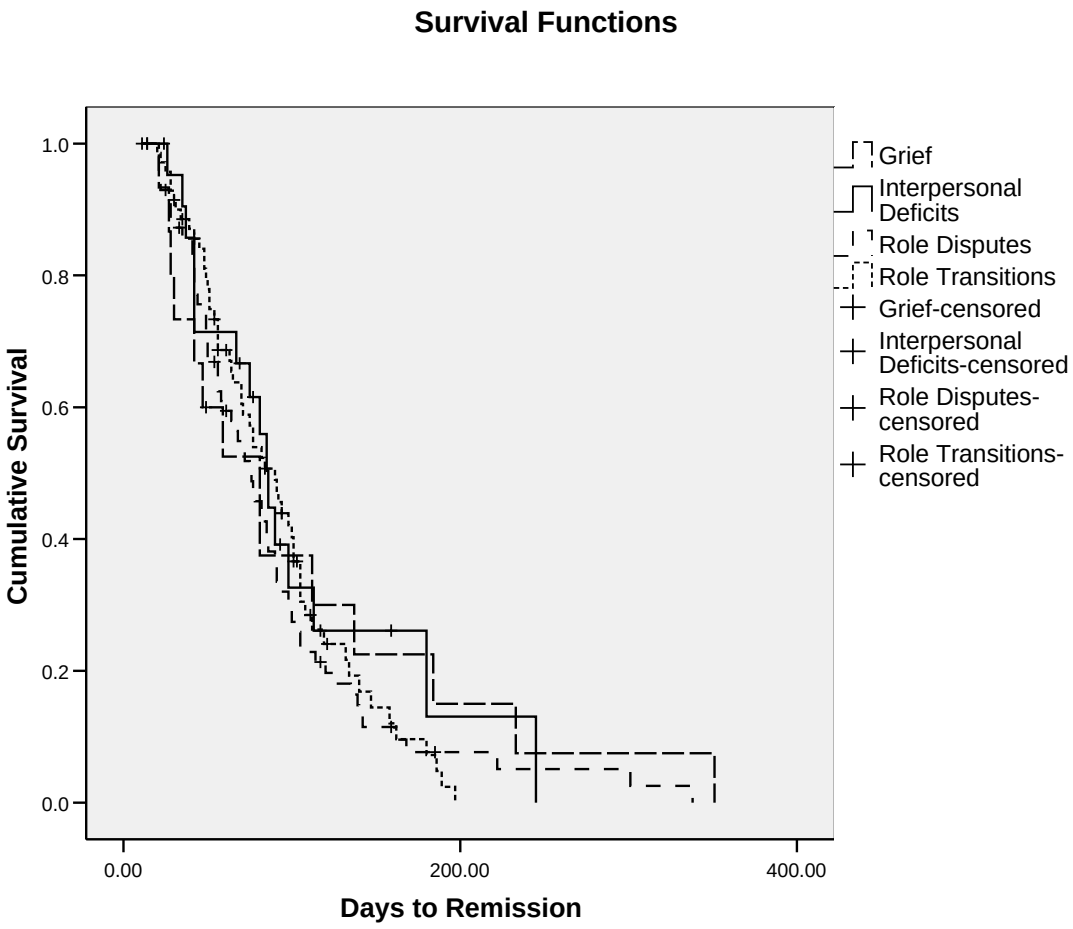

Figure 1. Days to remission by problem area.

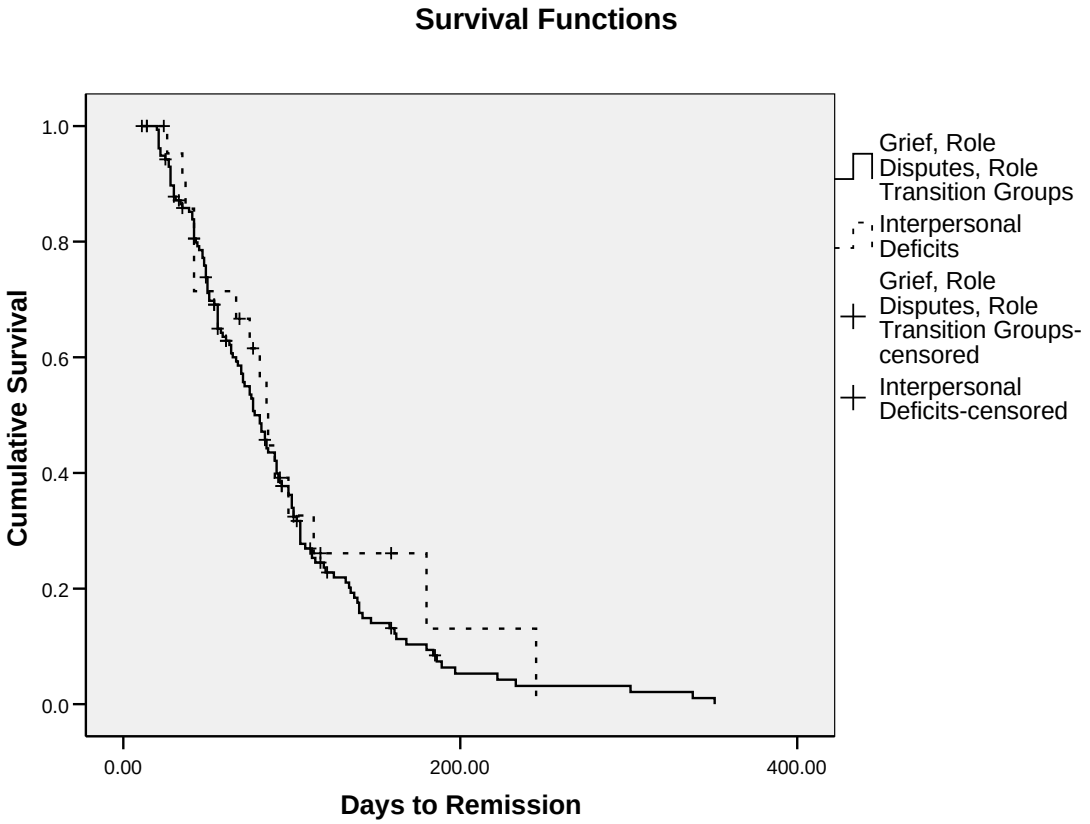

Figure 2. Days to remission comparing interpersonal deficits and the other three problem area groups.

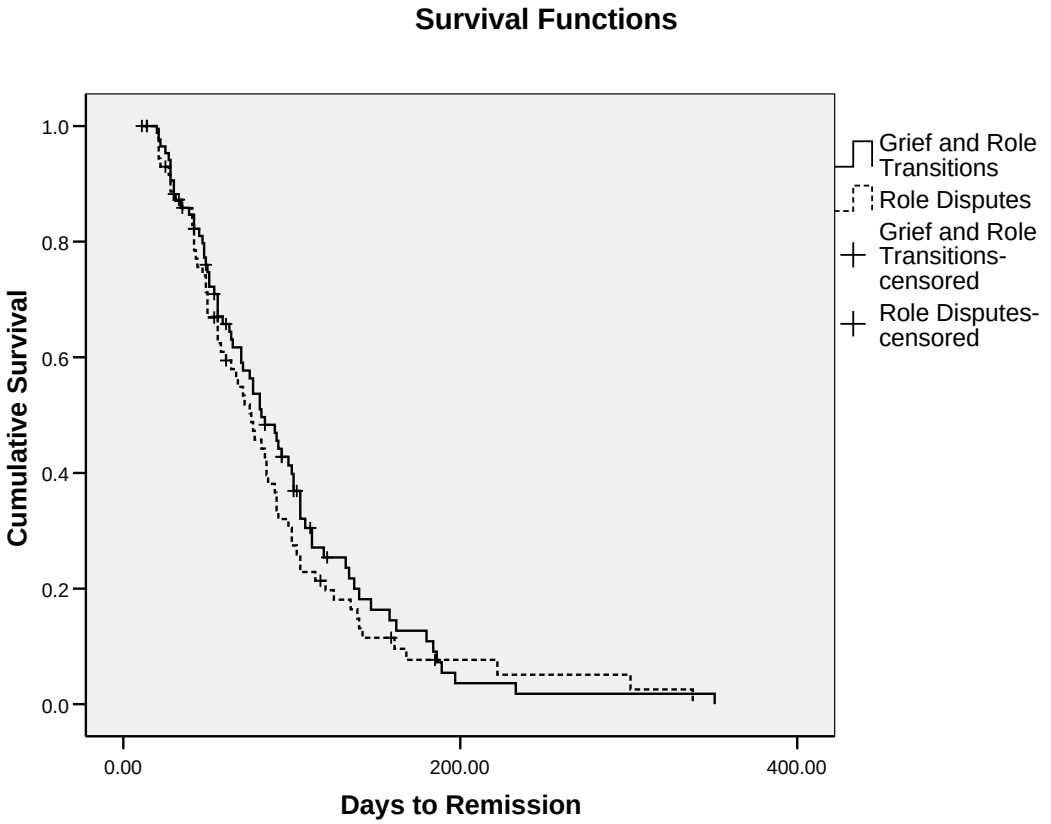

Figure 3. Days to remission comparing the role disputes problem area group with the grief and role transition problem area groups

remission between these two groups (X^2=0.773, p=0.379). Moreover, exploratory analyses revealed no significant differences when comparing the time to remission of the grief group and the other three groups (X^2=0.473, p=0.491) or the role transitions group and the other three groups (X^2=0.025, p=0.874).

The Cox Proportional Hazard Model was utilized to determine the effect of personality pathology, measured continuously, on time to remission. When entered into a univariate model it appears that endorsing a greater number of probes on the SCID-II is associated with a longer time to remission at a trend level (Exp(β)=0.992, p=0.056). This variable was excluded from the hierarchical model described above as it is so highly correlated with the categorical measure of personality pathology, as shown in Table 3. We also hoped to understand the potential effect of the addition of medication on a patient's time to remission. However, not all patients received medication, and the addition of medication occurred at varying time points depending on the patient's need; thus, we considered the addition of medication to be a time-varying covariate. In this case, the addition of medication was associated with a decreased time to remission (β=-0.78, p=0.0006).

We also hoped to understand if the addition of pharmacotherapy interacted with problem area assignment. Using the Cox Proportional Hazard Model we found that time to remission did not differ between patients whose treatment focused on interpersonal deficits and all other patients as a result of the addition of medication (β=0.44, p=0.41). Thus, assignment to the deficits problem area and the addition of medication did not interact significantly to produce an effect on time to remission.

Based on the fact that individuals who received medication experienced a shorter time to remission than patients who received IPT alone, we conducted exploratory analyses to determine if the addition of medication was associated with any patient characteristics. Medication was added to IPT in 38.7% of the overall sample with equal frequency across the four problem area groups (X^2=2.120, p=0.548). As well, the time points at which medication was added did not differ significantly among the four groups (X^2=2.224, p=0.527). We conducted chi-square analyses to determine which patient factors, if any, were associated with the addition of medication. It appears that the presence of additional lifetime or current Axis I disorders is associated with the addition of medication (X^2=5.402, p=0.020), which is expected given that additional pathology may increase the complexity of a patient's clinical picture. Males were also more likely to receive medication (X^2=9.248, p=0.002), suggesting that the treatment of depression in men may be more difficult than it is among women. In fact, in the overall study it appears that men were more difficult to treat with both IPT alone and pharmacotherapy alone (E. Frank, personal communication, July 30, 2008); thus, it may not be that men experience a poorer outcome with IPT, but that they are more difficult to treat in general.

As site was strongly correlated with a number of patient variables, we chose to examine differences among patients at each site. Patients at Pisa experienced a significantly shorter time to remission than at Pittsburgh (X^2=17.730, p=0.0001). Kaplan-Meier survival curves created to demonstrate this difference are shown in Figure 4. Moreover, it appears that patients at Pittsburgh and Pisa demonstrated different rates of remission reaching a trend level (X^2=3.012, p=0.083), with a tendency for more Pisa patients to achieve remission. Although the patients at each site received the same

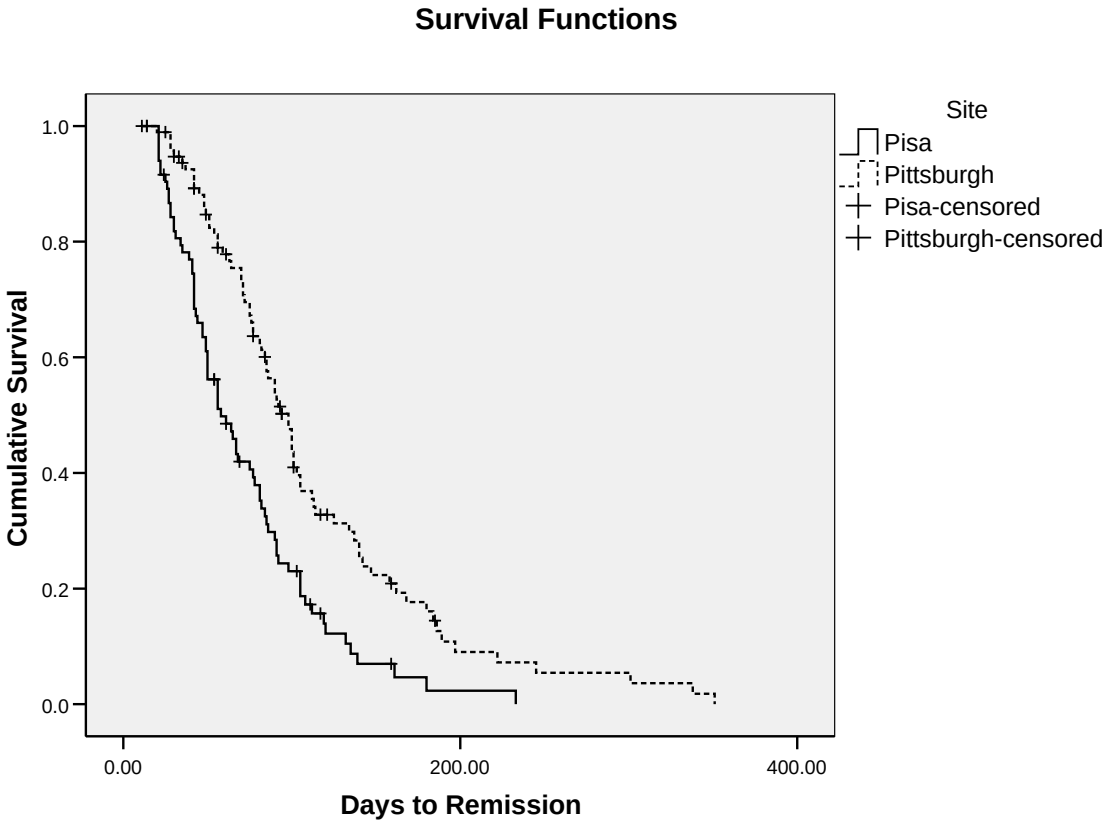

Figure 4. Time to remission among patients at Pittsburgh and Pisa.

psychotherapeutic treatment and there were no differences in the makeup of escitalopram used at each site, there may be some reasons for the significant differences in survival time. As is shown in Table 4, significantly fewer patients at Pisa required medication (X^2=28.639, p=0.0001), indicating that patients at Pisa experienced depression that was less difficult to treat. The Pittsburgh sample included more males (X^2=8.712, p=0.003) and male gender was associated with longer time to remission. Patients at Pittsburgh experienced more current and lifetime Axis I disorders (X^2=16.065, p=0.0001), higher levels of education (W=4938.500, p=0.0001), an earlier age of first depressive episode (W=7512.000, p=0.002), and more previous depressive episodes (W=4361.50, p=0.002), all variables associated with longer time to remission. Thus, in this sample site may be a proxy for these demographic and clinical variables.

Table 4. *Patient Characteristics by Site*

	Pittsburgh N=97	**Pisa N=84**
Mean Age (S.D.)	39.06 (1.34)	38.89 (1.33)
Sex (Female) [a]	60.8%	81.0%
Ethnicity (Caucasian)[b]	83.5%	97.6%
Mean Education Level in Years (S.D.)[c]	15.57 (0.27)	12.38 (0.32)
Employed/Student	75.3%	82.9%
Married or living with a Partner	34.0%	41.7%
Mean Age at First Depressive Episode (S.D.)[d]	24.16 (1.30)	28.92 (1.35)
Mean Number of Previous Episodes (S.D.)	3.00 (0.31)	2.96 (0.65)
Medication Added[e]	56.7%	17.9%
Baseline HRSD-17 Score	19.45 (0.39)	19.93 (0.38)
Other Current and Lifetime Axis I Disorders[f]	70.1%	40.5%
One or more Axis II Disorders	30.9%	28.9%
Remitted[g]	78.4%	88.1%

The two sites differed as follows:

[a] X^2=8.712, p=0.003
[b] X^2=10.01, p=0.002
[c] W=4938.5, p=0.0001
[d] W=7512.0, p=0.002
[e] X^2=28.64, p=0.0001
[f] X^2=16.07, p=0.0001
[g] X^2=3.012, p=0.083

9.0 DISCUSSION

In an effort to provide evidence for the specificity of IPT, we used survival analyses to compare time to remission among depressed patients whose treatment focused on each of the four problem areas. We found that patients in each of the four groups experienced similar times to remission. Contrary to prediction, those in the interpersonal deficits group did not experience a longer time to remission than the other patients combined, nor did patients whose treatment focused on role disputes experience a significantly longer time to remission than patients whose treatment focused on grief or role transitions. Patients in each of the four groups differed on a few demographic and clinical variables. We expected individuals in the interpersonal deficits group to report more personality pathology given our clinical experience and the fact that this group has been described as the most difficult to treat and more likely to suffer from characterologic challenges (Markowitz & Swartz, 2007; Stuart & Robertson, 2003; Weissman et al., 2000); however, we did not find strong evidence to support this hypothesis.

With regard to other differences among the groups, patients whose treatment focused on role transitions reported an earlier age at onset of their depression than patients in the grief group, while patients whose treatment focused on role transitions reported more additional Axis I pathology than patients in the role disputes groups. These

findings may indicate a more endogenous depression among patients in the role transitions group. Patients in the role transitions group also appear to be younger than the patients in the role disputes group, while it appears as though there are a higher proportion of patients who are married or living with a partner in the role disputes group than in the role transitions group.

Although historically a number of studies have indicated that demographic and clinical variables are not related to time to remission, in the present study education level, treatment site, and baseline depression score were predictive of time to remission. However, education level was no longer predictive of remission when site was added to the model; as site is highly correlated with education level, among other variables, we need to consider the fact that when site is added to the model it may mask the true association between these variables and time to remission. With regard to baseline depression score, we expect that patients who enter treatment with more severe depressive symptoms may experience a longer time to remission. Nonetheless, this does not seem to have much of an impact on our findings given that our four groups did not differ significantly on time to remission or on baseline depression score.

There are several possible explanations for the lack of significant differences between the interpersonal deficits group and other three groups on time to remission. We predicted that individuals in the interpersonal deficits group would report more personality pathology, and that perhaps this, in, turn, would explain the differences that we predicted would exist regarding time to remission. However, at least in this population, it appears that choice of the deficits area was not necessarily associated with personality pathology, whether measured continuously or categorically. Thus, the lack of

significant differences regarding time to remission may be the related to the fact that individuals in the interpersonal deficits group did not actually report a clinical picture that was complicated by significantly greater Axis II pathology.

Another explanation for the lack of differences may be the possibility that the individuals whose treatment focused on interpersonal deficits are not truly representative of those whose treatment should really focus on this interpersonal challenge. As Markowitz (2003) notes, clinicians are encouraged to focus on any problem area other than interpersonal deficits, if at all possible. He explains, "Interpersonal deficits are used as an IPT focus only when the alternative, life-event-based foci are absent, which is relatively rare. The term *interpersonal deficits* is a misnomer that might better be termed *no recent life events*. Not surprisingly, patients clustered in this category have been associated with poorer outcome than in the other IPT categories" (p. 849). Seemingly, it is less of a challenge for both clinician and patient to address more concrete and specific concerns related to a recent life event or a single specific role dispute, if present, than more pervasive, but less specific social deficits that have persisted chronically.

Thus, a patient whose treatment could or should focus on interpersonal deficits but who also presents with another potential focus of treatment, as did most of the deficits patients in this study, may be identified as having two treatment foci, usually with the deficits problem listed as the secondary focus if at all possible. In this project any individual whose treatment focused on interpersonal deficits either as a primary or secondary focus of treatment at any time point was included in the interpersonal deficits group. The rationale for this is that we believe it likely that these individuals truly suffer

from interpersonal deficits, but that treatment was conceptualized as focusing on another problem area because of the difficulty in working with an interpersonal deficits focus.

Nonetheless, we must acknowledge the possibility that individuals for whom interpersonal deficits was listed as a secondary focus may have spent the majority of their treatment working on one of the other three treatment foci, resulting in more successful and efficient resolution of their depression than might be seen if interpersonal deficits was the sole focus. Only two out of 181 patients in this study were assigned a problem area focus of interpersonal deficits without a secondary focus. One of these patients remitted after 86 days in the study with medication added on day 63, while the other terminated treatment after 24 days, reportedly because the patient did not respond to treatment. This lone deficits focus is not only rare, but in the other deficits cases, without conducting a session-by session analysis of treatment content, it is difficult to know how much impact an interpersonal deficits focus had on treatment if it was not the sole focus.

The fact that those individuals in whom an interpersonal deficits problem area was noted appear to have been treated successfully by *avoiding* the interpersonal deficits focus (despite the fact that social deficits may have been their true challenge), provides further support for IPT as an effective and flexible treatment for patients whose depression may not primarily be related to a life event. In the present study it appears that if a patient's depression can be resolved through work on a short-term interpersonal problem in the presence of social deficits, the current depressive episode may be resolved successfully. However, the treatment outcome of these patients may not be representative of patients whose treatment focused on interpersonal deficits alone. We also do not know whether challenges related to interpersonal deficits that were present all along but may

not have been addressed in treatment that was, instead, focused on an event-related problem, leave patients more vulnerable to subsequent relapse or recurrence. Even so, we may have reason to be encouraged; based on the two cases with a lone interpersonal deficits focus identified above, the patient who remitted did so in a time that is similar to the median survival time of all patients in the interpersonal deficits group (86 days for this patient vs. 81 days for the entire sample).

This project also predicted that those in the interpersonal deficits group would have significantly more personality pathology and personality diagnoses than those in the other three groups. We found only weak evidence to support this hypothesis. There was a non-significant trend for this group to have a higher probability of a personality disorders diagnosis. However, there were no differences among the groups with regard to personality pathology measured continuously with the SCID-II. Although organizing personality pathology into distinct diagnoses is clinically meaningful in most situations, perhaps the overall level of pathology reported by a patient has more of an effect on treatment of depression than whether this pathology is organized into disorders.

It appears that the majority of patients in this study with a personality disorder met criteria for a diagnosis in the cluster "C" category, such as avoidant, dependent, or obsessive-compulsive personality disorder. We would not expect individuals with cluster "C" disorders to be as difficult to treat as those with cluster "B" disorders; rather, the personality pathology symptoms endorsed by the majority of our patients naturally make them more isolative, avoidant, or anxious. It is possible that their personality pathology is concerning for them, but may not interfere directly with treatment.

Our fourth hypothesis stated that patients whose treatment focused on role disputes would fare worse with IPT than patients whose treatment focused on grief or role transitions. Our reasoning was based on the potential difficulty in incorporating the needs of a second individual (the individual with whom the patient has the dispute) into treatment. One possible explanation for the equal success among these patients may be the strength of the IPT strategies that are utilized in all problem areas, such as exploration of feelings, the use of the sick role, and improving communication. Perhaps the success of IPT seen in this project as a whole reflects the value of these more general strategies, regardless of problem area focus. Particularly in a disputes case, however, IPT is open to including the other party to the dispute in a few sessions of treatment, which may help to facilitate open communication, and may promote the understanding of both the patient and the significant other's feelings and nonreciprocal role expectations.

The fact that we did not find significant differences among the problem area groups is supported by the previous work of Wolfson and colleagues (1997) who found that IPT problem area is not associated with time to clinical response among older adults with depression. Although this earlier work did not include an interpersonal deficits group because of a small sample size in this problem area, the other three patient groups demonstrated similar treatment response. As in the present study, Wolfson and colleagues concluded that IPT, in the presence of carefully managed drug therapy, where appropriate, treats patients in each problem area with equal success.

Further analyses were conducted to explore how the addition of medication affected treatment outcome. The addition of medication indicated decreasing predicted survival time; that is, those who received medication appeared to remit more quickly than

those who received IPT alone. Including the addition of medication as a time-varying covariate allowed us see the effect of the addition of medication on time to remission *only* during the time period that the medication was added. It appears that patients who were not improving sufficiently with psychotherapy alone may have benefited from the addition of pharmacotherapy. We also did not find a significant difference in response to medication between the patients in the deficits group and all other patients, which could have had an effect on their time to remission. Thus, while the addition of medication may limit our ability to draw conclusions about the effect of IPT alone, this limitation appears to be consistent across all problem area groups.

In addition to medication, the continuous measure of personality pathology was the other variable entered into the Cox Proportional Hazards model independently to determine whether increased levels of this variable had an effect on time to remission. This variable was analyzed in a univariate model because a measure of personality pathology had already been entered into the stepwise model, and because the two variables were so highly correlated. In this univariate model, it appears that reporting a higher level of personality pathology was associated with an increased time to remission at a trend level, similar to the findings for the categorical measure of Axis II pathology.

Regarding site differences among the patients, the patients at Pisa experienced a significantly shorter time to remission than those at Pittsburgh. It appears that in this sample, site may be a proxy for other variables as these groups of patients differed significantly on a number of demographic and clinical variables that may have had an effect on time to remission. Lastly, it may also be important to examine the effects of informative or non-informative censoring on the success of treatment within each

problem area. Overall, most of the 31 censored patients' drop-out was informative; it is possible that patients whose censoring was informative would have affected the group's time to remission if they had not left the study.

9.1 LIMITATIONS

This study has several limitations. First, because patients are not randomly assigned to the problem areas under investigation, but collaboratively choose a treatment focus with their therapist based on their specific experience, the sample sizes of the grief and interpersonal deficits groups were much smaller than the role disputes and role transitions groups. This likely had an impact on our ability to detect a difference in survival times between the interpersonal deficits group and the other three groups. However, the median survival time for these groups was roughly 86 and 78 days, respectively; thus, even if we were able to detect a statistically significant difference this may not have been a clinically significant difference.

While clinically indicated and important for the larger goal of this study, the addition of pharmacotherapy limited our ability to interpret the differences among the problem area groups on time to remission based on treatment with IPT only. Although 61.3% of participants received IPT alone, 38.7% received medication as well when their depression proved difficult to treat with IPT alone. Despite analyses investigating the

effect of the pharmacotherapy, it nonetheless limits our ability to draw conclusions about the effectiveness of IPT alone. Moreover, there are some individuals for whom medication was not added at the exact point it was deemed necessary according to the study protocol, usually because a patient missed a scheduled visit. Thus, in a few cases there may have been an unavoidable lapse between when medication was deemed necessary and when it was actually given.

With regard to patient characteristics, the generalizability of these findings may be limited somewhat given that the sample was primarily made up of Caucasian individuals, and that patients who were severely depressed were excluded from the study. Moreover, it is somewhat difficult to account for the effect of patients who may have dropped out of the study for reasons related to their condition. While patients with informative censoring were split relatively evenly among the four problem area groups, we cannot know the effect that these patients would have had on our findings if they had remained in the study. Lastly, several of the patients in the study reported interpersonal challenges that fell into more than one problem area. Thus, we cannot determine how much time was spent discussing problems related to the patient's secondary problem area, which could have had an impact on the findings.

10. 0 CONCLUSIONS AND FUTURE DIRECTIONS

This study examined the relative time to remission among the four problem area groups of depressed individuals receiving IPT, in particular aiming to identify patient characteristics that may contribute to the differential efficacy of IPT among this sample. Individuals whose treatment focused on interpersonal deficits did not report significantly more personality pathology than the patients in the other three problem areas, whether measured continuously or categorically. Contrary to prediction, individuals in the interpersonal deficits problem area did not demonstrate a longer time to remission than the remainder of the sample, nor did individuals in the role disputes group demonstrate a longer time to remission than patients in the grief and role transitions groups. Thus, with the skillful use of IPT strategies and tactics and with careful medication management, where appropriate, patients in this study whose treatment focused on each problem area were treated with equal success by experienced IPT clinicians.

Future studies should continue to focus on characteristics of both patients and treatment to identify factors that may contribute to the differential efficacy of IPT in depressed adults. With a larger sample it would be possible to differentiate among the types of role transitions, the different individuals with whom a patient might be having a

role dispute, or the relationship between the patient and the individual who died in a grief case in order to determine whether these various relationships and situations have a differential effect on treatment outcome. Likewise, with a larger sample it would be possible to compare individuals whose treatment focused *primarily* on interpersonal deficits to those who focused secondarily on the deficits problem area; it is possible that there may be differences in time to remission among these groups depending on the extent to which an interpersonal deficits problem was the true focus of treatment. Finally, future studies may more accurately predict the time to remission of individuals whose treatment focuses on interpersonal deficits by asking clinicians to note the problem area of focus in treatment, as well as the problem area that the clinician would have liked to have focused on, if they differ.

BIBLIOGRAPHY

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders, text revision* (4th ed.). Washington, D.C.: Author.

Bearden, C., Lavelle, N., Buysse, D., Karp, J., & Frank, E. (1996). Personality pathology and time to remission in depressed outpatients treated with interpersonal psychotherapy. *Journal of Personality Disorders, 10*(2), 164-173.

Beck, A. T., Rush, A. J., Shaw, B. F., & Emery, G. (1979). *Cognitive therapy of depression*. New York: Guilford Press.

Beck, J. S. (1995). *Cognitive therapy: Basics and beyond*. New York: Guilford Press.

Bifulco, A., Brown, G. W., & Harris, T. (1987). Childhood loss of parent, lack of adequate parental care and adult depression: A replication. *Journal of Affective Disorders, 12*, 115-128.

Bowlby, J. (1982). *Attachment and loss* (2nd ed.). London: Hogarth Publishing.

Brown, G. W., & Harris, T. (1978). *Social origins of depression: A study of psychiatric disorder in women*. New York: Free Press.

Cyranowski, J. M., Frank, E., Winter, E., Rucci, P., Novick, D., Pilkonis, P. A., et al. (2004). Personality pathology and outcome in recurrently depressed women over 2 years of maintenance interpersonal psychotherapy. *Psychological Medicine, 34*, 659-669.

Elkin, I., Shea, M. T., Watkins, J. T., Imber, S. D., Sotsky, S. M., Collins, J. F., et al. (1989). National Institute of Mental Health Treatment of Depression Collaborative Research Program. General effectiveness of treatments. *Archives of General Psychiatry, 46*(11), 971-982.

Feske, U., Frank, E., Kupfer, D. J., Shea, M. T., & Weaver, E. (1998). Anxiety as a predictor of response to interpersonal psychotherapy for recurrent major depression: An exploratory investigation. *Depression and Anxiety, 8*(4), 135-141.

First, M. B., Gibbon, M., Spitzer, R. L., & Williams, J. B. W. (1997). *Structured Clinical Interview for DSM-IV Axis II Personality Disorders*. Washington, DC: American Psychiatric Publishing, Inc.

First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. W. (1997). *Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I)*. Washington, DC: American Psychiatric Publishing, Inc.

Frank, E., Kupfer, D. J., Buysse, D., Swartz, H. A., Pilkonis, P. A., Houck, P. R., et al. (2007). Randomized trial of weekly, twice-monthly, and monthly interpersonal psychotherapy as maintenance treatment for women with recurrent depression. *American Journal of Psychiatry, 164*(5), 761-767.

Frank, E., Kupfer, D. J., Perel, J. M., Cornes, C., Jarrett, D. B., Mallinger, A. G., et al. (1990). Three-year outcomes for maintenance therapies in recurrent depression. *Archives of General Psychiatry, 47*(12), 1093-1099.

Frank, E., Kupfer, D. J., Wagner, E. F., McEachran, A. B., & Cornes, C. (1991). Efficacy of interpersonal psychotherapy as a maintenance treatment of recurrent depression. Contributing factors. *Archives of General Psychiatry, 48*(12), 1053-1059.

Hamilton, M. (1960). A rating scale for depression. *Journal of Neurology, Neurosurgery, and Psychiatry, 23*, 56-62.

Harris, T., Brown, G. W., & Bifulco, A. (1986). Loss of parent in childhood and adult psychiatric disorder: The role of lack of adequate parental care. *Psychological Medicine, 16*, 641-659.

Henderson, S., Byrne, D. G., Duncan-Jones, P., Adcock, S., Scott, R., & Steele, G. P. (1978). Social bonds in the epidemiology of neurosis. *British Journal of Psychiatry, 132*, 463-466.

Hirschfeld, R. M. A. (1999). Personality disorders and depression: Comorbidity. *Depression and Anxiety, 10*, 142-146.

Hollon, S. D., Jarrett, D. B., Nierenberg, A. A., Thase, M. E., Madhukar, T., & Rush, J. (2005). Psychotherapy and medication in the treatment of adult and geriatric depression: Which monotherapy or combined treatment? *Journal of Clinical Psychiatry, 66*(4), 455-468.

Klerman, G. L., & Weissman, M. M. (1987). Interpersonal psychotherapy and drugs in the treatment of depression. *Pharmacopsychiatry, 20*, 3-7.

Klerman, G. L., Weissman, M. M., Rounsaville, B., J., & Chevron, E. S. (1984). *Interpersonal psychotherapy of depression*: Basic Books.

Leahy, R. L. (1996). *Cognitive therapy: Basic principles and applications*. Northvale, N.J.: J. Aronson.

Luecken, L. J. (2000). Attachment and loss experiences during childhood are associated with adult hostility, depression, and social support. *Journal of Psychosomatic Research, 49*, 85-91.

Luty, S. E., Joyce, P. R., Mulder, R. T., Sullivan, P. F., & McKenzie, J. M. (1998). Relationship between interpersonal psychotherapy and problem areas with temperament and character: A pilot study. *Depression and Anxiety, 8*, 154-159.

Markowitz, J.C. (2003). Interpersonal psychotherapy for chronic depression. *Journal of Clinical Psychology, 59(8),* 847-858.

Markowitz, J. C., Bleiberg, K. L., Christos, P., & Levitan, E. (2006). Solving interpersonal problems correlates with symptoms improvement in interpersonal psychotherapy: preliminary findings. *Journal of Nervous and Mental Disease, 194*(1), 15-20.

Markowitz, J. C., & Swartz, H. A. (2007). Case formulation in interpersonal psychotherapy of depression. In T. D. Eels (Ed.), *Handbook of psychotherapy case formulation* (2nd ed., pp. 221-250). New York: Guilford Press.

Markowitz, J. C., & Weissman, M. M. (2004). Interpersonal psychotherapy: principles and applications. *World Psychiatry, 3*(3), 136-139.

Miller, M. D. (2008). Using interpersonal psychotherapy (IPT) with older adults today and tomorrow: A review of the literature and new developments. *Current Psychiatry Reports, 10*, 16-22.

National Institute of Mental Health. (2000). Depression. Retrieved April 28, 2007, from http://www.nimh.nih.gov/publicat/depression.cfm

Parker, G., & Fletcher, K. (2007). Treating depression with the evidence-based psychotherapies: a critique of the evidence. *Acta Psychiatrica Scandinavica, 115*, 352-359.

Parker, G., Parker, I., Brotchie, H., & Stuart, S. (2006). Interpersonal psychotherapy for depression? The need to define its ecological niche. *Journal of Affective Disorders, 95*, 1-11.

Persons, J. B., Davidson, J., & Tompkins, M. A. (2000). *Essential components of cognitive behavior therapy for depression* (1st ed.). Washington, D.C.: American Psychological Association.

Reynolds, C. F., Frank, E., Perel, J. M., Imber, S. D., Cornes, C., Miller, M. D., et al. (1999). Nortriptyline and interpersonal psychotherapy as maintenance therapies for recurrent major depression: A randomized controlled trial in patients older than 59 years. *Journal of the American Medical Association, 281*(1), 39-45.

Reynolds, C.F., Miller, M.D., Pasternak, R. E., Frank, E., Perel, J.M., Cornes, C., et al. (1999). Treatment of bereavement-related major depressive episodes in later life: A controlled study of acute and continuation treatment with nortriptyline and interpersonal psychotherapy. *American Journal of Psychiatry, 152(2),* 202-208.

Shea, M. T., Pilkonis, P. A., Beckham, E., Collins, J. F., Elkin, I., Sotsky, S. M., et al. (1990). Personality disorders and treatment outcome in the NIMH Treatment of Depression Collaborative Research Program. *American Journal of Psychiatry, 147*(6), 711-718.

Shear, M.K., Frank, E., Houck, P.R., Reynolds, C.F., 3rd (2005). Treatment of complicated grief: a randomized controlled trial. *Journal of the American Medical Association, 293*(21)*,* 2658-2660.

Skodol, A. E., Stout, R. L., McGlashan, T. H., Grilo, C. M., Gunderson, J. G., Shea, M. T., et al. (1999). Co-occurrence of mood and personality disorders: A report from the Collaborative Longitudinal Personality Disorders Study (CLPS). *Depression and Anxiety, 10*, 175-182.

Sotsky, S. M., Glass, D. R., Shea, M. T., Pilkonis, P. A., Collins, J. F., Elkin, I., et al. (1991). Patient predictors of response to psychotherapy and pharmacotherapy: Findings in the NIMH Treatment of Depression Collaborative Research Program. *American Journal of Psychiatry, 148*(8), 887-1008.

Stuart, S., & Robertson, M. (2003). *Interpersonal psychotherapy: A clinician's guide*. New York: Oxford University Press.

Sullivan, H. S. (1953). *The Interpersonal Theory of Psychiatry*. New York: WW Norton & Company.

Wampold, B. E. (2005). Establishing specificity in psychotherapy scientifically: Design and evidence issues. *Clinical Psychology: Science and Practice, 12*, 194-197.

Weiss, R. S. (1975). *Marital separation*. New York: Basic Books.

Weissman, M. M. (1994, June). Cross-national data on the epidemiology of bipolar disorder. In M. M. Weissman (Chair), *Epidemiology and clinical course*. Symposium conducted at the First International Conference on Bipolar Disorder, Pittsburgh, Pennsylvania, USA.

Weissman, M. M., Klerman, G. L., Prusoff, B. A., Sholomskas, D., & Paidan, N. (1981). Depressed outpatients: Results one year after treatment with drugs and/or interpersonal psychotherapy. *Archives of General Psychiatry, 38*, 51-56.

Weissman, M. M., & Markowitz, J. C. (1994). Interpersonal psychotherapy: Current status. *Archives of General Psychiatry, 51*, 599-606.

Weissman, M. M., Markowitz, J. C., & Klerman, G. L. (2000). *Comprehensive guide to interpersonal psychotherapy*. New York: Basic Books.

Weissman, M. M., Prusoff, B. A., DiMascio, A., Neu, C., Gokolaney, M., & Klerman, G. L. (1979). The efficacy of drugs and psychotherapy in the treatment of acute depressive episodes. *American Journal of Psychiatry, 136*(4B), 555-558.

Weissman, M. M., Prusoff, B. A., & Klerman, G. L. (1978). Personality and the prediction of long-term outcome of depression. *American Journal of Psychiatry, 135*(7), 797-800.

Wolfson, L., Miller, M. D., Houck, P. R., Ehrenpreis, L., Stack, J. A., Frank, E., et al. (1997). Foci of interpersonal psychotherapy (IPT) in depressed elders: Clinical and outcome correlates in a combined IPT/nortriptyline protocol. *Psychotherapy Research, 7*(1), 45-55.

World Health Organization. (2007). Depression. Retrieved April 28, 2007, from http://www.who.int/mental_health/management/depression/definition/en/

Zuckerman, D. M., Prusoff, B. A., Weissman, M. M., & Padian, N. S. (1980). Personality as a predictor of psychotherapy and pharmacotherapy outcome for depression outpatients. *Journal of Consulting and Clinical Psychology, 48*(6), 730-735.